Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV

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Appendix B, Table 5. Characteristics of Protease Inhibitors (Last updated December 18, 2019; last reviewed December 18, 2019) (page 1 of 4)

The older PIs FPV, IDV, NFV, SQV, and TPV are no longer commonly used in clinical practice and have been removed from this table. Please refer to the July 10, 2019 version of the guidelines (found in the archived guidelines section of AIDS*info*) or to the FDA product labels for information regarding these drugs.

Generic Name (Abbreviations) *Trade Name*	Formulations	Dosing Recommendations[a]	Elimination/ Metabolic Pathway	Serum Half-Life	Adverse Events[b]
Atazanavir (ATV) *Reyataz* (ATV/c) *Evotaz* **Note:** Generic products of ATV are available.	**Reyataz:** • 150, 200, and 300 mg capsules • 50 mg oral powder/packet **Generic:** • 100, 150, 200, and 300 mg capsules **Evotaz:** • ATV 300 mg/ COBI 150 mg tablet	**Reyataz** *In ARV-Naive Patients:* • (ATV 300 mg plus RTV 100 mg) once daily; *or* • ATV 400 mg once daily • Take with food. *With TDF or in ARV-Experienced Patients:* • (ATV 300 mg plus RTV 100 mg) once daily • Unboosted ATV **is not recommended**. • Take with food. *With EFV in ARV-Naive Patients:* • (ATV 400 mg plus RTV 100 mg) once daily • Take with food. **Evotaz**: • One tablet once daily • Take with food. • The use of ATV/c **is not recommended** for patients who are taking TDF and who have baseline CrCl <70 mL/min (see Appendix B, Table 10 for the equation for calculating CrCl). For dosing recommendations for patients who are also receiving H2 antagonists and PPIs, refer to Table 21a.	**ATV:** • CYP3A4 inhibitor and substrate • Weak CYP2C8 inhibitor • UGT1A1 inhibitor **COBI:** • CYP3A inhibitor and substrate • CYP2D6 inhibitor Dose adjustment is recommended in patients with hepatic insufficiency (see Appendix B, Table 10).	7 hours	Indirect hyperbilirubinemia PR interval prolongation. First degree symptomatic AV block has been reported. Use with caution in patients who have underlying conduction defects or who are on concomitant medications that can cause PR prolongation. Cholelithiasis Nephrolithiasis Renal insufficiency Serum transaminase elevations Hyperlipidemia (especially with RTV boosting) Skin rash Hyperglycemia Fat maldistribution An increase in serum creatinine may occur when ATV is administered with COBI.

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Generic Name (Abbreviations) *Trade Name*	Formulations	Dosing Recommendations[a]	Elimination/ Metabolic Pathway	Serum Half-Life	Adverse Events[b]
Darunavir (DRV) *Prezista* (DRV/c) *Prezcobix*	**Prezista**: • 75, 150, 600, and 800 mg tablets • 100 mg/mL oral suspension **Prezcobix**: • DRV 800 mg/ COBI 150 mg tablet Also available as part of the STR Symtuza (DRV/c/ TAF/FTC)	**Prezista** *In ARV-Naive Patients or ARV-Experienced Patients with No DRV Mutations:* • (DRV 800 mg plus RTV 100 mg) once daily • Take with food. *In ARV-Experienced Patients with One or More DRV Resistance Mutations:* • (DRV 600 mg plus RTV 100 mg) twice daily • Take with food. Unboosted DRV **is not recommended**. **Prezcobix:** • One tablet once daily • Take with food. • **Not recommended** for patients with one or more DRV resistance-associated mutations. • Coadministering Prezcobix and TDF **is not recommended** for patients with baseline CrCl <70 mL/min (see Appendix B, Table 10 for the equation for calculating CrCl). See Appendix B, Table 1 for dosing information for Symtuza.	**DRV:** • CYP3A4 inhibitor and substrate • CYP2C9 inducer **COBI:** • CYP3A inhibitor and substrate • CYP2D6 inhibitor	15 hours when combined with RTV 7 hours when combined with COBI	**Skin Rash:** DRV has a sulfonamide moiety, however incidence and severity of rash are similar in those with or without a sulfonamide allergy; Stevens-Johnson syndrome, toxic epidermal necrolysis, acute generalized exanthematous pustulosis, and erythema multiforme have been reported. Hepatotoxicity Diarrhea, nausea Headache Hyperlipidemia Serum transaminase elevation Hyperglycemia Fat maldistribution An increase in serum creatinine may occur when DRV is administered with COBI.

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Generic Name (Abbreviations) *Trade Name*	Formulations	Dosing Recommendations[a]	Elimination/ Metabolic Pathway	Serum Half-Life	Adverse Events[b]
Lopinavir/ Ritonavir (LPV/r) *Kaletra* **Note:** LPV is only available as a component of an FDC tablet that also contains RTV.	**Kaletra:** • LPV/r 200 mg/50 mg tablets • LPV/r 100 mg/25 mg tablets • LPV/r 400 mg/100 mg per 5 mL of oral solution. Oral solution contains 42% alcohol.	**Kaletra:** • LPV/r 400 mg/100 mg twice daily, *or* • LPV/r 800 mg/200 mg once daily. However, once-daily dosing **is not recommended** for patients with three or more LPV-associated mutations, pregnant women, or patients receiving EFV, NVP, carbamazepine, phenytoin, or phenobarbital. *With EFV or NVP in PI-Naive or PI Experienced Patients:* • LPV/r 500 mg/125 mg tablets twice daily (use a combination of two LPV/r 200 mg/50 mg tablets plus one LPV/r 100 mg/25 mg tablet to make a total dose of LPV/r 500 mg/125 mg), *or* • LPV/r 533 mg/133 mg oral solution twice daily **Food Restrictions** *Tablet:* • Take without regard to meals. *Oral Solution:* • Take with food.	CYP3A4 inhibitor and substrate	5–6 hours	GI intolerance, nausea, vomiting, diarrhea Pancreatitis Asthenia Hyperlipidemia (especially hypertriglyceridemia) Serum transaminase elevation Hyperglycemia Insulin resistance/ diabetes mellitus Fat maldistribution Possible increase in the frequency of bleeding episodes in patients with hemophilia PR interval prolongation QT interval prolongation and Torsades de Pointes have been reported; however, causality could not be established.
Ritonavir (RTV) Norvir **Note:** Generic is available. Although RTV was initially developed as a PI for HIV treatment, RTV is currently used at a lower dose of 100 mg to 200 mg once or twice daily as a PK enhancer to increase the concentrations of other PIs.	**Norvir:** • 100 mg tablet • 100 mg soft gel capsule • 80 mg/mL oral solution. Oral solution contains 43% alcohol. • 100 mg single packet oral powder Also available as part of the FDC tablet Kaletra (LPV/r)	**As a PK Booster (or Enhancer) for Other PIs:** • RTV 100–400 mg per day in one or two divided doses (refer to other PIs for specific dosing recommendations). **Food Restrictions** *Tablet:* • Take with food. *Capsule and Oral Solution:* • To improve tolerability, take with food if possible.	CYP3A4 > 2D6 substrate Potent CYP3A4 and 2D6 inhibitor Inducer of UGT1A1 and CYPs 1A2, 2C8, 2C9, and 2C19	3–5 hours	GI intolerance, nausea, vomiting, diarrhea Paresthesia (circumoral and extremities) Hyperlipidemia (especially hypertriglyceridemia) Hepatitis Asthenia Taste perversion Hyperglycemia Fat maldistribution Possible increase in the frequency of bleeding episodes in patients with hemophilia

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[a] For dose adjustments in patients with hepatic insufficiency, see Appendix B, Table 10.

[b] Also see Table 17.

Key: ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; AV = atrioventricular; COBI = cobicistat; CrCl = creatinine clearance; CYP = cytochrome P; DRV = darunavir; DRV/c = darunavir/cobicistat; EFV = efavirenz; FDA = Food and Drug Administration; FDC = fixed-dose combination; FPV = fosamprenavir; FTC = emtricitabine; GI = gastrointestinal; IDV = indinavir; LPV = lopinavir; LPV/r = lopinavir/ritonavir; msec = millisecond; NFV = nelfinavir; NVP = nevirapine; PI = protease inhibitor; PK = pharmacokinetic; PPI = proton pump inhibitor; RTV = ritonavir; SQV = saquinavir; STR = single-tablet regimen; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TPV = tipranavir; UGT = uridine diphosphate glucuronyl transferase